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ON THE

DEVELOPMENT OF FAT.

BY

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In a paper published in the Medical Gazette more than two years ago, (Jan. 1848) I stated my belief that the presence of a nucleus is not an essential condition in the developement of a fat cell, "but that it may arise as a minute vesicle filled with oil, and continue to enlarge by the intussusception of oily matter supplied to it, the envelope expanding and gaining strength in proportion as the contents accumulate." Since then I have made numerous observations on the condition of fat cells, and have by them been led to maintain more exclusively the view I then proposed, so that now I consider it to occur very rarely, if ever, that a fat cell is developed in any other way than that just mentioned. I proceed to detail some of the observations which seem to justify this conclusion.

In the muscular tissue of a sprat I found fatty matter disposed in the following manner. Long rows and groups of oil globules lay between the fibres: they did not appear to possess distinct envelopes, and were occasionally seen fused together: there were also masses of apparently true fat cells, which did not coalesce together, and were not affected by ether. Among those thus treated were numerous vesicles of every size down to $\frac{1}{5000}$ inch, or even less. From the examination of this specimen it seemed certain that here, at least, oil was directly separated from the blood, and that, as it collected into drops of varying size, these became surrounded with an envelope.

In a perch I found a fat mass from the abdomen, consisting of vesicles of very various sizes embedded in a fibrous tissue, which, however, was very delicate and scanty. There was no trace of developement cells nor nuclei to be seen anywhere. The vesicles varied in size from $\frac{1}{600}$ to $\frac{1}{4000}$ inch, or less, and, save in respect of magnitude, were all of precisely similar appearance. On ether being added, a good deal of oil was extracted in the form of large drops; but very many vesicles, small as well as large, remained unaltered. I conclude that the small fat vesicles, as well as the larger, are provided with envelopes,—that they are not mere oil-drops.

In a piece of adipose tissue from the abdomen of a frog I found no trace of developement cells, nor of pre-existing nuclei. The vesicles were of all sizes, from $\frac{1}{600}$ inch to $\frac{1}{6000}$ inch. They were not aggregated together, but lay near each other in a kind of blastematous nidus. They were not altered by ether. I should state that in both this observation and the preceding the animals were rather emaciated than otherwise, but I do not think this materially impairs the evidence they afford, that fat vesicles exist of all sizes, down to a magnitude not exceeding that of an ordinary nucleus

In a small bird I examined a portion

of fat from between the muscles of the thigh immediately under the skin. It consisted of lobular masses, which were in great part made up of vesicles of various size; together with these, and grouped around them in vast numbers, were small oil vesicles, or drops, which were globular and well-defined, and only differed from the larger by their inferior size. They were of all dimensions, from nearly the size of fat cells down to a magnitude almost too minute for measurement.

There was no appearance of the developement of fat vesicles from pre-existing cells, or of oil-drops being aggregated around nuclei, but several masses were seen which appeared to consist of oily molecules in process of fusion together.

In the mesentery of a young rook I found several small masses of fat, consisting of vesicles which varied in size from $\frac{1}{1500}$ to $\frac{1}{10000}$ inch. The larger were clustered over with minute ones, and these last were often seen grouping themselves together, as if about to fuse and constitute a larger vesicle. No trace could be discerned of developement cells or nuclei. Ether was added, but did not extract any oily matter. The vesicles remained unaltered. I measured one after the addition of this agent, which did not exceed $\frac{1}{5000}$ inch, and there were many similar. Thus these were not mere oil-drops. Acetic acid did not alter the appearance of the vesicles. I remarked that in the situation of a lobule of fat there is a thickening of the membrane (peritoneum), apparently by the deposition of an amorphous or faintly granular blastema. This deposit is accurately limited, and does not exist in the interspaces between adjoining lobules. In it, probably the exudation of oil and the development of oil vesicles takes place.

In the mesentery of a mouse, I observed a small vessel with groups of fat vesicles, as I conceive in process of developement, lying along its side. Towards the further extremity the groups consisted of comparatively few and small oil drops; as one advanced towards the other end the drops became larger, and presented more decidedly the aspect of oil filled vesicles, still, however, clustered over with minute drops. Here the conclusion seems quite inevitable, that the fat vesicles, which in parts closely adjacent were of the usual size and form, were developed by aggregation and fusion of oil drops, and the formation of an envelope round them.

In a child, aged only a few weeks, who died of sclerema, in the Hôpital des Enfans Trouvés, at Paris, I observed similar appearances in the fat about the capsule of the kidney; minute drops were seen grouping themselves together, but there appeared no trace of preexisting cells in which the oil-drops should be deposited. I could follow out a regular series from fat vesicles of the ordinary size down to the most minute.

In the mesentery of a human fœtus at term, there were several little fat masses visible to the naked eye; in one small group extending along the side of a vessel, I measured some minute vesicles which did not exceed $\frac{1}{8000}$th inch in diameter; yet they exhibited a distinct dark edge, and appeared in all respects similar to large ones, $\frac{1}{1000}$th inch in diameter: none of the vesicles presented any trace of a nucleus.

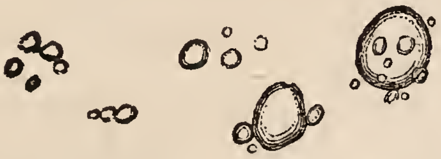
In a fœtal rabbit, near term, I found in the inguinal fold a small quantity of lobulated adipose tissue. The fat cells were small, very few so large as $\frac{1}{1000}$th inch, and from this size down to the merest points there were seen vesicles or drops of all intervening magnitudes. Often the larger cells were seen clustered over with minute drops which appeared to be about to add themselves to the enlarging vesicle. There was often also a small quantity of semi-oily, semi-granular matter diffused around the cells, which probably constitutes a kind of blastema to them. Pressure on the specimen did not destroy the fat vesicles, or cause oil to exude, so that it seems certain the minute vesicles were not mere drops of oil forced out of the larger. Ether being added, extracted rapidly a large quantity of oil which was seen floating about in great drops: it must have affected large vesicles as well as small, the quantity was so great. When ether was added to a portion of the mesentery of an adult rabbit containing fat, no such effect was produced; the vesicles remained unaltered. There were no pre-existing development cells in which oil was found, nor did it appear that oily molecules aggregated together around nuclei, but I observed large cells which might have been regarded as containing a nucleus: I convinced myself, however, pretty certainly, that this was not really a nucleus, but a small mass of granular matter on the *outside* of the true vesicle, but contained with it in a kind of accidental envelope.

I have examined several times fat vesicles taken from persons who died in a state of very great emaciation, but the results of these observations have differed a good deal.

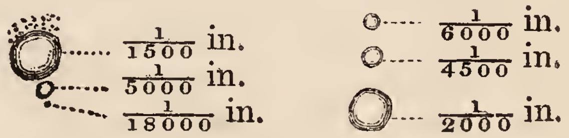
Sometimes there appeared to be no envelope, but the oil-drop diminished in size was surrounded by a small quantity of granular matter. Sometimes the envelope was distinct, and the cavity contained only a very small oil drop with some faint amorphous matter and transparent fluid: sometimes in the half-emptied vesicle there were traces of a nucleus more or less distinct: this last circumstance I mention as being of some importance, though I do not feel absolutely certain as to the correctness of the observation.

A large fat-vesicle from a perch, with smaller ones clustering round it: the diameter of the large one, $\frac{1}{600}$ in.; that of the smallest, $\frac{1}{12000}$.

Fat-vesicles from frog, varying in diameter from $\frac{1}{1200}$ in. to $\frac{1}{3000}$ or less.



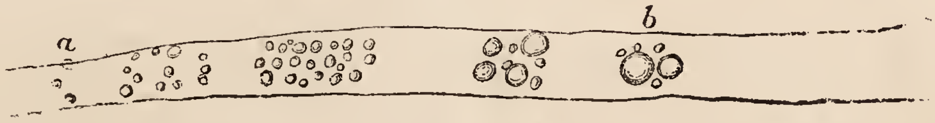
Fat-vesicles from mesentery of a young rook: they are of all intervening magnitudes from $\frac{1}{1500}$ to $\frac{1}{10000}$ in.



Fat-cells from fœtal rabbit.

A mass consisting of minute oil-drops in a state of imperfect fusion together, from a small finch.

A small group of minute fat-vesicles from mesentery of fœtal rabbit, lying quite isolated: the largest is not more than $\frac{1}{4000}$ in.



A small vessel from mesentery of mouse, with groups of minute fat-vesicles along its wall, which tend to coalesce and form larger ones: the diameter of the smallest, at *a*, $\frac{1}{6000}$ in.; at *b*, $\frac{1}{2000}$ in.: near to *b*, meshes of ordinary fat-vesicles existed.

On considering the evidence now brought forward, I think, if it be accepted, it can scarcely remain doubtful that the fat vesicles are ordinarily developed without pre-existing cells or nuclei: the process seems to consist in the gradual separation of oil from the blood, or rather from the exuded liquor sanguinis, whereby oil-drops are formed, at first minute, afterwards enlarging both by addition and coalescence, and soon becoming enclosed in an envelope of proteine material. This envelope is at first very feeble, perhaps scarcely organized, but afterwards acquires considerable strength, and sometimes persists after the absorption of the oily contents. The original imperfect state of the envelope is well shown by the different effect of ether on the adipose tissue in the fœtus and in the adult, the oil in the one case being rapidly extracted from the vesicles; in the other little, if at all. The formation of the envelope appears to be the only act of organizing power that takes place in fat, the only circumstance that entitles it to rank as a tissue; in some fishes probably the fat is in great measure merely so much exuded oil lying in the interstices of the tissues, and does not become truly organized.

Whether a nucleus is at some time formed in the fat vesicles or not, I do not know: if this should occasionally be the case it would show that the vesicles had attained a higher degree of organization, becoming thus true nucleated cells.

In conclusion, I wish to draw attention to a circumstance which I have already dwelt upon in the paper before referred to—viz., that in two instances, that of the adipose tissue and that of the pulmonary aerating surface, where the secretion product is of a very simple nature, and certainly pre-exists in the blood, the analogues of the epithelium of glands are absent or very slightly developed. This points unequivocally to the importance of the epithelium in the process of secretion; a fact which at the present day is trite and common, but which our advancing chemical knowledge seems to render only less easy of explanation.

The constituent principles of the secretions, it seems most probable, pre exist in the blood, and can be formed without the glands, as shown in the experiments of extirpation and in the results of disease; yet the glands possess a peculiar structure which seems to be developed very much in proportion to the complex character of the secretion, and which in many of the lower animals is seen to contain the elaborated product, while in the higher classes it seems to be chiefly or entirely an albuminous substance, and does not evidently contain the secretion. The great difficulty seems to be to understand why the epithelium should be in so great a degree an albuminous substance. If the growing cells extracted from the blood merely or chiefly the constituents of the secretion, as they often seem to do in the lower animals, the process, though essentially mysterious in its nature, would in its stages be clear; or, if we did not find the secretions formed in the blood, it might be assumed, without much risk of error, that the albuminous epithelium underwent a chemical decomposition, breaking up into the constituents of the secretion, and a complementary material, which returned to the blood: but to explain how the epithelial cells, withdrawing from the blood little else than albumen for their own formation, are yet so essentially concerned in the elimination of the more complex secretions, is a great enigma. It may be one day solved, and all the apparent contradictions and differences shown to be dependent on some great general law; but from this we are far at present; and, in default of any simpler arrangement, we must, I believe, recognise the following diverse conditions of the secretory process:—

1. Secretions pre-existing in the blood removed from it in an almost purely physical manner—*ex.* oil, carbonic acid.

2. Secretions pre-existing in the blood in a more or less perfect state, but requiring under ordinary circumstances a peculiar epithelial apparatus for their removal—*ex.* the principles of the urine, bile, saliva, &c.

3. Secretions which do not pre-exist in the blood, and which appear to be *formed* by the action of gland-cells—*ex.* semen, gastric juice, mucus, pigmentum nigrum.

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